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NOVEL FRAGMENTATION IN BUPHANISINE⁺
VIA INTERPRETATION OF ITS HIGH RESOLUTION MASS SPECTRUM²

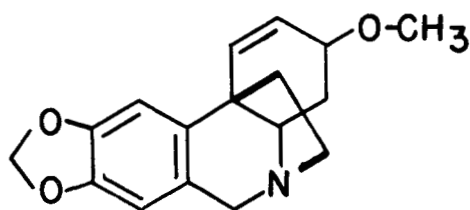
SIR:

The successful application of the low resolution mass spectro-metric method to many structural studies in the indole and dihydro-indole alkaloids reflect the proclivity of the nitrogen atom to dominate the major modes of molecular fragmentation.^(3,4) Recently, Biemann et al.^(5,6) have proposed an "element map" for the presentation of high resolution mass spectral data in an attempt to allow structural inferences to be drawn from grouping the observed ions according to their heteroatomic content. Thus, in the case of deoxydihydro-N_b-methy-lajmaline and voacangine, the overwhelming predominance of entries within the nitrogen heteroatomic groups was interpreted as demonstrating that the heteroatom, nitrogen, "is intimately built into the carbon skeleton, making it impossible to produce ions without heteroatoms to any appreciable extent." High resolution mass spectral data of ajmaline, ajmalidine and related alkaloids⁽⁷⁾ would bear out this conclusion.

In this laboratory consideration of the matrix tabulation (Table 1) of the elemental compositions and fragment intensities⁽⁸⁾ for buphanisine (I) has revealed that such an assumption regarding the "intimately built-in" nature of the bicyclic bridgehead nitrogen in this Amaryllidaceae alkaloid could have led to erroneous structural correlations with its high resolution mass

spectrum, were it an alkaloid of unknown structure. This surprising feature is apparent from the observation that the most abundant fragments are found in the CHO₃ column, demonstrating that the bicyclic bridgehead nitrogen is eliminated in a neutral fragment from the molecular ion.⁽⁹⁾

Rational accounting for this unexpected observation may be depicted by the fragmentation sequence in Scheme 1 showing the elimination of the alicyclic nitrogen as 55 mass units (m.u.) of composition C₃H₅N and 55+15 m.u. (C₄H₈N).⁽¹⁰⁾ Benzylic cleavage (5,6-bond) of buphanisine (I), with charge retention on the tropilium moiety thus generated, forms species a, which can

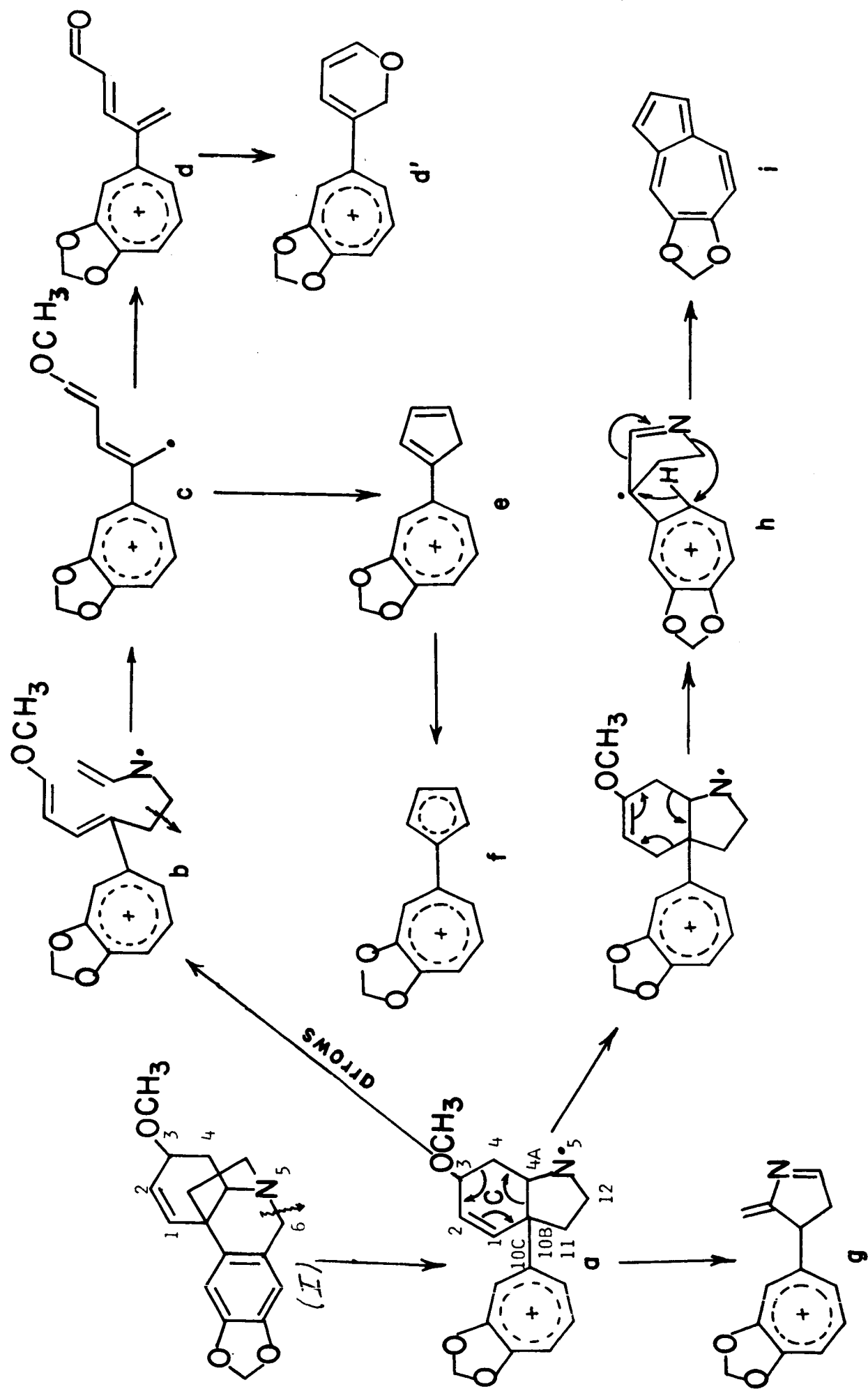


I

undergo retro-Diels-Alder fission of ring C, resulting in the "open" molecular ion, b.⁽¹¹⁾ Loss of azabutadiene by simple fission of the 11,12-bond in b forms the conjugated allylic radical ion, c (M-55), of composition C₁₄H₁₄O₃.

Now facile expulsion of a methyl radical from fragment c produces the highly unsaturated, methylenedioxytropilium ion, d (M-70), of composition C₁₃H₁₁O₃. A large metastable peak is observed in the conventional mass spectrum for the transition 230 → 215. This loss of a methyl radical may be assisted energetically by the formation of the pyrane structure, d'.

SCHEME I



Cyclization of fragment c with subsequent loss of a methoxy radical results in ion e ($C_{13}H_{11}O_2$) which could readily lose a hydrogen radical to form the cyclopentadienyl species f.

It should be noted that several fragments of lesser abundance do contain the alicyclic nitrogen: (1) loss of methyl radical from the molecular ion; (2) loss of methoxyl radical from the molecular ion generating an allylic carbonium ion at C-3; (3) expulsion of ethylene (C-11,C-12); and (4) the removal of a C_4H_7O and a C_5H_8O species from ring C to give fragments g and h. Fragment h may cyclize with concomitant loss of neutral HCN to form a series of ions of compositions $C_{11}H_{10-8}O_2$ via expulsion of hydrogen radicals to form the fully aromatic methylenedioxy-azulenium ion i.

The correlations postulated in this communication are further substantiated by analogous results for amaryllisine,⁽¹²⁾ buphanidrine, crinine and their dihydroderivatives,⁽¹³⁾ which will be reported in a full paper in this series.⁽¹⁴⁾

These results represent the first example where the neutral nitrogen-containing moiety, azabutadiene, is eliminated directly from a bicyclic bridgehead position. Other examples of nitrogen heteroatom elimination upon electron impact occur as ammonia,⁽¹⁵⁾ hydrogen cyanide,⁽¹⁶⁾ methylene imine,⁽⁹⁾ from monocyclic systems or acyclic side chains;⁽⁸⁾ and dihydroisoquinoline⁽⁹⁾ from a bicyclic system. Thus, caution must be exercised in the interpretation of the population distributions arranged according to heteroatomic content arising from high resolution mass spectrograms.

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2. This communication represents Part III in the Berkeley series, Mass Spectrometry in Molecular Structure Studies. For Part II, see A. L. Burlingame in Advances in Mass Spectrometry, vol. III, Pergamon Press, in press.
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8. High resolution mass spectra were determined with a Mattauch-Herzog double-focussing mass spectrometer/spectrograph (C.E.C. 21-110) with simultaneous, permanent registration of the entire spectrum on a photographic plate (Ilford Q-2). Samples were introduced from an all glass inlet system operated between 180 and 200°C and determined with ionizing voltage at 70 e.v. and ionizing current in the range 100-300 microamp. Completely automatic photoplate data reduction was accomplished via feeding both digitized line positions (in microns) and plate blackening (in percent transmission) directly onto an IBM format compatible magnetic tape memory from a high precision recording microphotometer. The magnetic tape was processed directly by an IBM 7044 or 7094 digital computer which calculates accurate mass data and then provides the elemental compositions and intensities of all ions in the spectrogram in an appropriate output format. Perfluorokerosine was used as mass standard. Details of development and operation of our fully automatic data reduction system will be reported, see A.L. Burlingame and Richard W. Olsen, Anal. Chem., in preparation.
9. Loss of a substituted dihydroisoquinoline moiety from the tetrahydroprotoberberine alkaloids has been proposed to explain the conventional mass spectra (A. L. Burlingame, Ph.D. Thesis, M.I.T., December, 1962, pp. 87-91); M. Ohashi, J. M. Wilson, H. Budzikiewicz, M. Shamma, W. A. Slusarchyk and C. Djerassi, J. Am. Chem. Soc., 85, 2807 (1963).

10. Preliminary results were presented at the Institute of Petroleum/ASTM Mass Spectrometry Symposium, Paris, September 14-18, 1964, by one of us (A.L.B.)
- 11a. The retro-Diels-Alder fission of ring C is further corroborated by the occurrence of the less abundant fragment of composition $C_{15}H_{14}O_3$, which represents the loss of the aza-allyl radical ($\dot{C}H_2=CH-NH\cdot$) from the molecular ion, b.
- b. The possible representation of the open form, b, as a benzyl derivative cannot be excluded, but representation as a methylenedioxytropilium ion, d, is consistent with the subsequent loss of formaldehyde to give the substituted tropolone ion ($C_{12}H_9O_2$) and the loss of carbon monoxide from the tropolone to yield a substituted phenyl type ion ($C_{11}H_9O$), processes which have been postulated as operative in methylenedioxybenzyl systems which can form the tropilium ion on electron impact [B. Willhalm, A. F. Thomas and F. Gautschi, Tetrahedron, 20, 1185 (1964); Biemann, Mass Spectrometry, op. cit., p. 308]. Loss of formaldehyde during tropilium ion formation has been confirmed by appearance potential measurements [J. M. S. Tait, T. W. Shannon and A. G. Harrison, J. Am. Chem. Soc., 84, 4 (1962)].
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15. K. Biemann, Mass Spectrometry, Op. cit., p. 97.
16. Ibid., p. 108, 302.